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April 26, 2007.
Signed: /Leslie Jennings/

Atty Docket No: **UCLA-P041**
Client Ref: **2000-093-1**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

JOSEPH R. PISEGNA

Application No.: **09/671,764**

Filed: **09/27/2000**

For: **USE OF A PENTAGASTRIN TO INHIBIT GASTRIC ACID SECRETION OR AS A DIURETIC**

Examiner: **CHIH MINH KAM**

Art Unit: **1656**

Confirmation No: **7433**

DECLARATION UNDER 37 C.F.R. §1.132

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. §1.132

I JOSEPH R. PISEGNA, M.D. declare and state as follows:

1. I am currently an Associate Professor of Medicine associated with the UCLA Medical Center. I specialize in gastroenterology and digestive diseases. My area of research expertise is in the regulation of gastric acid secretion.

2. I am also an inventor of the subject matter claimed in the above-identified patent application.

3. It is my understanding that the Examiner has rejected the claims in the above-identified patent application, alleging that we have not provided experimental data to establish that gastrin or pentagastrin can increase the efficacy of a gastric H+/K+-ATPase pump inhibitor (PPI) as presently claimed.

4. The experimental data described below supports our assertion that gastrin and/or pentagastrin can enhance the activity of a PPI.

5. Gastric acid measurements were performed in urethane anesthetized mice using the pylorus ligation model. In brief, overnight fasted WT and PAC1-/- mice were anesthetized with urethane 1.25g/kg via i.p. injection. After a laparotomy, the pylorus was ligated. A small incision was made in the mouse foregut, and a double-lumen gastric cannula was inserted. A 30-gauge needle connected with PE-10 tubing was placed into sapheous vein for injection of rat gastrin-I and/or pantoprazole with indicated dosage with an interval of 20 minutes. Continuous intragastric perfusion of saline (pH 7.0) was performed at a speed of 0.3ml/min. The effluents were collected at 10min intervals, and then titrated back to pH 7.0 with 0.001 N NaOH base. The dose for the experiment was as follows:

Rat Gastrin I: 250ug/kg;
Pantoprazole sodium: 10mg/kg;
Injection interval: 15minutes.

6. The resulting data are shown below in Figure 1.

7. As illustrated in Figure 1, at the indicated time point (arrow) mice were treated with either PPI (Pantoprazole sodium) alone (closed circles) versus PPI plus gastrin (open squares). Acid secretion was measured at 10-minute intervals. The two groups of mice had similar basal acid outputs prior to administration of the test agents. In mice administered PPI plus gastrin there was an enhanced reduction of gastric acid secretion compared to the mice administered only PPI. This difference in acid outputs was observed at over 120 minutes of time. These results indicate that intravenous gastrin when administered together with a PPI increases the efficacy of PPI-induced gastric acid inhibition.

8. One of skill in the art would readily appreciate that similar results can be obtained using gastrin or pentagastrin and using other PPIs.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 4-25-07

Respectfully submitted,

Dr. Joseph Pisegna

EFFICACY OF PPI ALONE VERSUS PPI+GASTRIN ON GASTRIC ACID SECRETION IN MICE

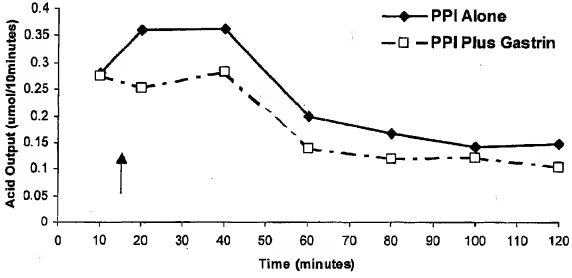

Fig. 1